Precise featuring the size, surface charge and dye loading of highly monodisperse silica nanoparticles for developing ¨stealth¨ charged vehicles for nanomedicine

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Chemical modification of silica particles leads to a variety of applications in biomedical fields, such as, drug delivery, gene therapy and molecular imaging. In this work, sequential modification of size, surface charge, dye loading and colloidal stability in physiological media of monodisperse silica nanopartciles by one-pot adapted Stöber[1] method is described. The radius of the silica cores with narrow sizes distributions SD≥10% can be systematically controlled in the range of 20 to 300 nm by the water/TEOS ratio in the starting reaction. The surface charge modification were done by covalently functionalization the negavite surface hydroxyl groups with the (3-aminopropyl)trimethoxysilane (APTES), considered to induce a positive surface charge by siloxane bonds to the silica surface and exposing amine ends. Our results allowed systematically controll the surface charge from -42.0 mV to 45.0 mV and tunning the isoelectric point (IEP) from 5.7 to 8.6. In addition, the degree of amine grafting on the passivated surface was determined by the ninhydrin assay. The primary or secondary amines attached on the surface, reacted with nynhydrine, yielding a bright purple complex known as Ruhemann´s purple. The numbers of amine molecules per surface grafted obtained were 1.50 to 4.43 NH_2 molecules/nm^2. The fluorescent molecules were incorporated during the particle formation by imposition of the dye on the silica network via the formation of a covalent bond between the dye and a silane coupling agent (APTES). Dyes having an isothiocyanate functional group were incorporated following a thiourea-linkage and the ones having succinimidyl esters followed a carboxamide-linkage. The colloidal stability in physiological media was also evaluated, in order to improve systemic circulation time and shield the nanoparticle surface from aggregation, opzonization and phagocytosis. A coating-step strategy using an inert polymer the mPEG5K silane were done in order to confer steric stabilization, surface charge protection and resistance for the interactions with components of the blood stream, imparting “stealth” properties.

References

[1] Stöber, W., A. Fink, and E. Bohn, *Controlled growth of monodisperse silica spheres in the micron size range.* Journal of Colloid and Interface Science, 1968. **26**(1): p. 62-69.

Figures

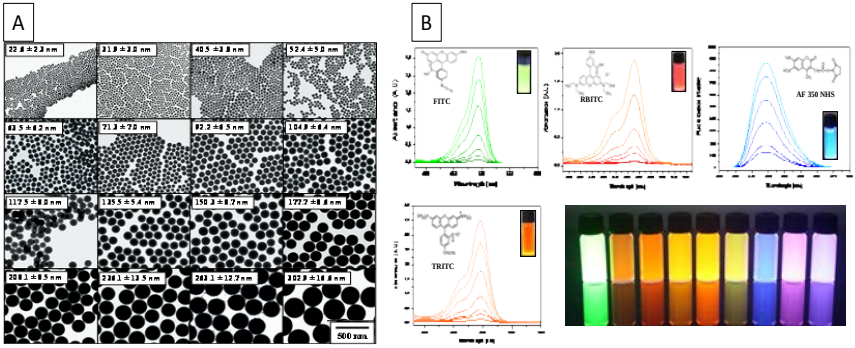

Figure 1: (A) Transmission electron microscopy images of the silica nanoparticles obtained in the one-pot adapted Stöber synthesis of silica nanoparticles. Particle size increase from 22.6 ± 2.30 nm to 302.9 ± 16.6 nm. (B) Uv-Vis absorption spectra of the 50nm silica nanoparticles with different core dyes concentration. Fluorescein isothiocyanate (FITC), Rhodamine B isothiocyanate (RBITC), Tetramethylrhodamine isothiocyanate (TRITC) and Alexa Fluor 350 NHS ester (AF350NHS). Different Rainbow-like nanoparticles can be achieved mixing different molar cuantities of dye-silane precursors duing the one-pot modified Stöber synthesis.